REMARKS

This document is filed in reply to the Office Action dated December 11, 2003 ("Office Action").

Applicants have amended claims 1 and 4 to specify that the recited set of nucleic acids include a third pair of primers, each containing an oligo-nucleotide selected from the non-structural protein 2 gene region of respiratory syncytial virus, e.g., SEQ ID NOs: 12 and 14, or SEQ ID NOs: 13 and 15. Support for the amendments to claims 1 and 4 can be respectively found in original claim 3, lines 6-7 and original claim 5, lines 6-7. These amendments have necessitated the amendments to clams 2, 3, and 5, which depend from claim 1 or 4. Applicants have also narrowed the scope of claim 9 by deleting the phrase "a second nucleic acid containing a second oligo-nucleotide selected from the non-structural protein gene region of influenza virus A" and recited the phrase in new claim 27, which depends from claim 9 and does not introduce any new matter. Finally, Applicants have amended the dependency of claims 10 and 12 so that these two claims now depend from claim 27. No new matter has been introduced.

Claims 1-27 are pending. Among them, claims 18-26 have been withdrawn from further consideration for being drawn to a non-elected invention. In this connection, Applicants would like to point out that the Examiner mistakenly stated in the Office Action Summary that "claims 12-26 is/are withdrawn from consideration." Indeed, as acknowledged by the Examiner in the Office Action, only "[c]laims 18-26 ... are withdrawn." See page 2, lines 6-7. Applicants therefore request that the error be corrected. Claims 1-17 and 27 are now under examination. Reconsideration of this application is requested in view of the following remarks:

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-3, 6, and 9-11, drawn to nucleic acids, for lack of written description. It is his position that the claimed nucleic acids "[include] variants for which no written description is provided...[and are] represented in the specification by only the particularly named SEQ ID Nos." See the Office Action, page 4, lines 9-11.

Applicants disagree and discuss independent claim 1 first. This claim covers a set of nucleic acids that include three pair of primers, which contain oligo-nucleotides selected respectively from (1) the hemagglutinin-neuraminidase gene region of human parainfluenza virus 2 (HPIV2), (2) the hexon gene region of adenovirus (ADV), and (3) the non-structural protein 2 gene region of respiratory syncytial virus (RSV). The Specification describes examples for each pair of primers[1] and points out that they hybridize to the corresponding gene regions under high stringent conditions, allowing one to amplify the region flanked by them. See, e.g., the Specification, the paragraph bridging pages 11-12.

Applicants submit that the Specification provides sufficient written description for claim 1. See the U.S. Patent and Trademark Office's guidelines on the subject: Synopsis of Application of Written Description Guidelines, www.uspto.gov/web/menu/written.pdf ("Guidelines"). The first pair of primers recited in claim 1 is discussed first.

Example 9 of the Guidelines illustrates a hypothetical situation that mirrors the present case. Just as in Example 9, the first pair of primers are drawn to two "isolated nucleic acid[s] that hybridize to [sequences from the hemagglutinin-neuraminidase gene region of HPIV2] under highly stringent conditions and [amplify an HPIV2 segment flanked by the two nucleic acids]. Just as in Example 9, "[the first pair of primers are] drawn to a genus of nucleic acids all of which must hybridize with [the sequences] and must [amplify the HPIV2 segment]." Furthermore, just as in Example 9, "[t]here [are two] species disclosed ([SEQ ID NOs: 5 and 7, and SEQ ID NOs: 6 and 7]) that [are] within the scope of the claimed genus" and "[t]here is actual reduction to practice of the disclosed species." Example 9 then provides the following guidance to examiners:

> "Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization conditions set forth in the claim yield structurally

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[1] Examples for each pair of primers are listed below:
the first pair of primers: SEQ ID NOs:5 and 7, and SEQ ID NOs:6 and 7, see pages 9-10, Table 1;
the second pair of primers: SEQ ID NOs:24 and 26, SEQ ID NOs:24 and 27, and SEQ ID NOs:25 and 27, see pages 9-10, Table 1;
the third pair of primers: SEQ ID NOs:12 and 14, and SEQ IN NOs:13 and 15, see pages 9-10, Table 1.

similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the ... function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.
Conclusion: The claimed invention is adequately described."

In view of the very clear instructions from the Guidelines and the teachings in the Specification, Applicants submit that the first pair of primers meet the written description requirement. By the same token, the second pair of primers and the third pair of primers recited in claim 1 also meet the requirement. It follows that claim 1 meets the requirement.

Each of claims 2-3 depends from claim 1 and recites four more pairs of primers. For the same reasons set forth above, they also meet the written description requirement.

Independent claim 6 covers a set of nucleic acids that include one or more of three nucleic acids amplified from (1) a respiratory syncytial virus (RSV) nucleic acid template with a first pair of primers, each containing an oligo-nucleotide selected from the non-structural protein 2 gene region; (2) an influenza virus A (INFA) nucleic acid template with a second pair of primers, each containing an oligo-nucleotide selected from the non-structural protein gene region; and (3) an influenza virus B (INFB) nucleic acid template with a third pair of primers, each containing an oligo-nucleotide selected from the hemagglutinin-neuraminidase gene region. Independent claim 9 covers a set of nucleic acids including (1) a first nucleic acid containing a first oligo-nucleotide selected from the non-structural protein 2 gene region of RSV, (2) a second nucleic acid containing a second oligo-nucleotide selected from the hemagglutinin-neuraminidase gene region of INFB, or (3) both of the first and the second nucleic acids. All of the claimed nucleic acids can be used as amplification primers or hybridization probes for detecting one of the just-mentioned three viruses and must hybridize to one of the just-mentioned three genes under high stringent hybridization conditions. See, e.g., the Specification, the paragraph bridging pages 11-12. For the same reasons set forth above, Applicants submit that claims 6 and 9 also meet the written description requirement. So do claims 10 and 11, which depend from claim 9 and further specify the lengths of the claimed nucleic acids.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-17 for indefiniteness. It is his position that "[i]n the sequence listing of elected SEQ ID NOs: 20, 35, 38, 39, 49, and 50, there are ambiguity codes such as K meaning G or T/U as well as other codes. However, the claims are indefinite as to whether they are intended to encompass a mixture of primers for the primers with ambiguity codes or a single primer with one of the two sequences." See the Office Action, page 7, lines 5-8. Applicants disagree.

First, the sequences in the sequence list are the same as those in Tables 1-3 of the Specification. The Specification clearly teaches that "[t]he sequence of each [primer or probe] is listed [in Tables 1-3]." See, e.g., page 5, line 24; page 6, line 9; and page 12, line 21. In other words, each of the listed sequences represents one particular primer or probe instead of a mixture. Thus, there is nothing indefinite about claims 1-17 for reciting one or more of the sequences.

In addition, Applicants would like to point out that the sequence listing was prepared according to the rules of 37 CFR 1.821. The rules incorporate by reference the World Intellectual Property Organization (WIPO) Standard ST. 25 (1998), including the use of the above-mentioned "ambiguity codes," such as K. See, MPEP 2422, Table 1. According to MPEP 2422.03, "[t]he rules, in general, or the use of sequence identifiers throughout the specification and claims, specifically, should not raise any issues under 35 U.S.C. 112, first or second paragraphs." Thus, claims 1-17 should not be rejected under 35 U.S.C. 112, second paragraph.

For the reasons set forth above, Applicants submit that claims 1-17 meet the definiteness requirement.

Rejection under 35 U.S.C. § 102(a)

The Examiner rejected claims 9-11 for being anticipated by Grondahl et al., J. Clin. Microbiol., 1999, 37(1):1-7 ("Grondahl"). See the Office Action, page 8, lines 8-9. According to the Examiner, Grondahl teaches a set of nucleic acid selected from the nonstructural protein gene of influenza virus A, which are 20 nucleotides in length. Applicants have amended claim 9,

from which claims 10 and 11 depend indirectly, and submit that the amendment has overcome this rejection

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected all of the pending claims for obviousness on three grounds. Applicants address each ground below:

I

The Examiner rejected claims 1-2 and 9-11 as being obvious over Grondahl in view of Echevarria et al., J. Clin. Microbio.,1998, 36(5): 1388-1391 ("Echevarria"). See the Office Action, page 9, lines 6-8. Applicants disagree and discuss independent claims 1 and 9 first.

As discussed above, amended claim 1 covers a set of nucleic acids that include 3 pair of primers. Among them is a third pair of primers, each containing an oligo-nucleotide selected from the non-structural protein 2 gene region of RSV. In other words, this pair of primers is RSV-specific.

According to the Examiner, Echevarria teaches a pair of primers containing sequences selected from the hemagglutinin-neuraminidase gene region of HPIV2, and Grondahl teaches 6 pairs of primers containing sequences selected respectively from: (1) the hexon gene of ADV, (2) the hemagglutinin-neuraminidase gene of human parainfluenza virus 1 (HPIV1), (3) the 5' noncoding region of the fusion protein gene of human parainfluenza virus 3 (HPIV3), (4) the F1 subunit of the fusion glycoprotein gene of RSV, (5) the non-structural protein gene of INFA, and (6) the non-structural protein gene of INFB. It is the Examiner's position that it would have been obvious to one skilled in the art to combine the pairs of primers taught in Grondahl and Echevarria to obtain a set of nucleic acids of claim 1.

Applicants note that (1) Echevarria is silent on any RSV-specific primers, and (2) the RSV-specific primers taught in Grondahl were derived from the F1 subunit of the fusion glycoprotein gene of RSV. In contrast, the RSV-specific primers recited in claim 1 is derived from the RSV non-structural protein 2 gene region. Since Echevarria and Grondahl, combined

or alone, do not teach or suggest a pair of primers derived from the RSV non-structural protein 2 gene region, as required in claim 1, they do not render claim 1 obvious.

Claim 9 is drawn to a set of nucleic acids including, among others, a first nucleic acid containing a first oligo-nucleotide selected from the non-structural protein 2 gene region of RSV. For the same reasons set forth above, this claim is not obvious over Grondahl and Echevarria.

Thus, claims 1 and 9 are non-obvious over Grondahl and Echevarria. So are claims 2 and 10-11, all of which depend from claims 1 and 9, directly or indirectly.

II

The Examiner rejected claims 3 and 6 as being obvious over Grondahl in view of Echevarria, Osiowy et al., J. Clin. Microbio. 1998, 36:3139-3154 ("Osiowy"), and Zuckerman et al., J. Virol. Methods, 1993, 44:35-44 ("Zuckerman"). See the Office Action, page 11, lines 12-16. Applicants respectively traverse the Examiner's ground for rejection below and discuss claim 3 first.

Claim 3, dependent from claims 1 and 2, is drawn to a set of nucleic acids that include, among others, (1) a third pair of primers, each containing an oligo-nucleotide selected from the non-structural protein 2 gene region of RSV, and (2) a seventh pair of primers, each containing an oligo-nucleotide selected from the hemagglutinin-neuraminidase gene region of INFB.

As discussed in Part I above, Grondahl and Echevarria do not teach or suggest a pair of primers, each containing an oligo-nucleotide selected from the non-structural protein 2 gene region of RSV. The Examiner also correctly acknowledged that they do not teach primers having sequences from the hemagglutinin-neuraminidase gene of INFB (see page 11, lines 18-21). Nonetheless, the Examiner alleged that Osiowy and Zuckerman rectified the deficiency of Grondahl and Echevarria.

First, the Examiner pointed out that Osiowy teaches a pair of primers containing oligo-nucleotides selected from the nucleocapside (N) gene of RSV and then concluded that it teaches the third pair of primers recited in claim 1, which contains an oligo-nucleotide selected from the non-structural protein 2 gene region of RSV. To support his conclusion, the Examiner alleged that "the nucleocapside [is] also called nonstructural protein 2." See the Office Action, page 11,

lines 19-20. Applicants disagree. In fact, contrary to the Examiner's allegation, nucleocapside is not nonstructural protein 2. See, e.g., Fig.2 of Hacking et al., J Infect. 2002 Jul;45(1):18-24 (attached hereto as Exhibit A).

Second, it is the Examiner's position that Zuckerman teaches the seventh primers recited in claim 3, which have sequences from the hemagglutinin-neuraminidase gene of INFB. More specifically, he referred to pages 35 and 37 of Zuckerman, which teaches primers "corresponding to the INFB HA-1 coding region." The Examiner would be correct only if the term "HA1" referred to the hemagglutinin-neuraminidase gene. However, Zuckerman explicitly teaches that the term "HA1" refers to the hemagglutinin gene, instead of the hemagglutinin-neuraminidase gene. See, page 35, the Summary, lines 3-4. Thus, the Examiner position is untenable.

For the two facts set forth above, Applicants submit that the 4 cited references, in any combinations, do not render claim 3 obvious.

Claim 6 covers a set of nucleic acids that include, among others, (1) a first nucleic acid obtained from amplification of an RSV template with a first pair of primers, each containing an oligo-nucleotide selected from the non-structural protein 2 gene region; and (2) a third nucleic acid obtained from amplification of an INFB nucleic acid template with a third pair of primers, each containing an oligo-nucleotide selected from the hemagglutinin-neuraminidase gene region. It is therefore not rendered obvious by the 4 references for the same reasons presented above

III

Finally, the Examiner rejected claims 4, 5, 7, 8, and 12-17 over Grondahl in view of Echevarria, Osiowy, Zuckerman, Buck et al., Biotechniques, 1999, 27(3): 528-536 ("Buck"), U.S. Patent 5,374,717 to Rota et al., ("Rota"), and 6 GenBank Accession Nos, i.e., X55803, X57559, M18759, M73260, M11486, and M12594. See the Office Action, the paragraph bridging pages 12-13.

Claims 4, 5, 7, 8, and 12-17 recite SEQ ID NOs: 1-57. According to the Examiner, Rota and the 6 GenBank Accession Nos teach sequences that cover these SEQ ID NOs. As such, he concluded that "[i]t would be prima facie obvious to one of ordinary skilled in the art ... to combine [Grondahl, Echevarria, Osiowy, and Zuckerman and to select primers] from the 6

GenBank Accession Nos and U.S. Patent 5,374,717" to make the SEQ ID NOs. Applicants disagree

As an example, Applicants will discuss GenBank Accession No X55803, which teaches a sequence of the HPIV1 hemagglutinin-neuraminidase gene, containing SEQ ID NO:1 recited in claims 5 and 8. Note that the prior art sequence and SEQ ID NO:1 are 1866 and 22 nucleotides in length, respectively. The prior art sequence contains 1845 different 22-nucleotide sequences (1845 = 1866 - 22 + 1). Thus, even if one skilled in the art would set out to select a 22-nucleotide primer from this prior art sequence, as alleged by the Examiner, he would have to choose it from as many as 1845 candidate primers. Since all of the above 11 references cited by the Examiner, combined or alone, do not suggest choosing SEQ ID NO: 1 from the 1845 candidates, they do not render obvious claims reciting SEQ ID NO: 1, i.e., claims 5 and 8.

By the same token, all of the 11 cited references do not render the other rejected claims obvious. Indeed, the sequences taught in the other 5 GenBank Accession Nos and Rota are at least 856 nucleotides in length. Accordingly, one would have to choose one primer from at least 835 candidates.[2]

The Examiner also relied on Buck to support the rejection against claims 4, 5, 7, 8, and 12-17. This reference describes a survey showing that 164 primers selected from a 300 bp target sequence functioned well in sequencing a template. As such, the Examiner concluded that "Buck provides direct evidence that all primers [selected from a target sequence] would be expected to function." See the Office Action, page 15, lines 17-18. Applicants disagree.

First, according to Buck, "[the] template was pre-selected to contain a test sequence lacking obstacles to sequence extension and purified by double banding in CsCl-ethidium bromide isopycnic density gradients." The purification eliminates any potential non-specific annealings of the primers to contaminating sequences. In contrast, the nucleic acids of claims 4, 5, 7, 8, and 12-17 are used to amplify and detect unpurified viral sequences from samples, e.g., throat swab specimens containing myriads of sequences (including those from the human

[2] According to the Examiner, the sequence of GenBank Accession No M11486 (856 nucleotides in length) covers SEQ ID NOs:16 and 18, (both 22 nucleotides in length). The total number of 22-nucleotide candidate primers can be chosen from the 856-nucleotide sequence is 835 (835 = 856 - 22 + 1).

genome). It is unreasonable to extrapolate data obtained on an artificial and purified sequence to a natural and unpurified sequence. Thus, the Examiner's conclusion is untenable.

In view of the above reasons and amendments, Applicants submit that all pending claims are non-obviousness over the cited references and request that the rejection be withdrawn.

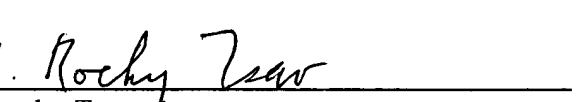
CONCLUSION

Applicant submits that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is definite, sufficiently described, novel, and non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Enclosed is a $110 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 4-12-04



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